evidence of vasculitis was present in three of four biopsy specimens.

Bacterial overgrowth in the bypassed bowel segments and immune complex formation in response to the excess of bacterial antigens have been suggested as the possible causes of extraintestinal manifestations of the bowel bypass syndrome. The response to antibiotic drugs, evidence of vasculitis in three cases and detection of immune complexes in two cases suggest that a similar pathogenesis may account for papulopustular eruptions seen in bowel bypass patients. However, present therapy is empirical and no single regimen has been consistently beneficial.

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PUVA Carcinogenesis

THE EFFICACY OF PUVA treatment with orally given 8-methoxypsoralen (P) combined with long-wave ultraviolet radiation (UVA) for the clearing of severe psoriasis has been established. The palliative nature of this therapy is evidenced by the recurrence of psoriasis despite continued maintenance therapy once a week or less frequently. Treatment of recurrent psoriasis with PUVA on a more frequent schedule is a common procedure, which over the years may result in a large cumulative UVA irradiation dose expressed in terms of joules per cm.^{2} The safe upper limit of ultraviolet A dosage from PUVA therapy is not known at this time.

The risk of carcinogenesis from chronic exposure to PUVA has been an early concern. In laboratory animals given large doses of psoralen topically or intraperitoneally plus UV light, a high incidence of squamous cell carcinomas and fibrosarcomas has occurred. The oral administration of psoralen in animals, once thought to be photoprotective, may also produce these tumors in conjunction with UV light. More and more evidence has emerged from in vitro studies that PUVA can be carcinogenic depending on the dose. PUVA has a mutagenic effect in bacterial systems. Sister chromatid exchanges, which have been employed as a cytologic means for the detection of potential carcinogens, have been observed in PUVA cells in vitro but not in vivo. It is known that exposure to nonionizing radiation and to PUVA can affect components of the immune system, which may play a role in photocarcinogenesis.

In humans, a type of epidermal dystrophic change similar to that which occurs in actinic keratoses has been observed in about half of 37 patients treated with PUVA. These changes, which were present at clearing and after a year of therapy, may indicate that cells have been altered genetically by somatic mutation. Whether the epidermal dystrophy is transient or represents a persistent abnormality is being investigated further.

Clinical evidence of PUVA carcinogenicity has emerged from a multicenter follow-up study of more than 1,300 patients. Stern and co-workers documented a total of 48 cases of basal cell and squamous cell carcinomas in 30 patients treated with PUVA during an average observation period of 2.1 years. A significant increase in the incidence of cutaneous cancer was found in patients with previous skin cancers and in those with a history of exposure to ionizing radiation, when compared with the expected risk for an age-sex and geographically-matched population. Of particular concern was an inverse in the expected ratio of basal cell epitheliomas to squamous cell carcinomas, as well as the frequent occurrence of squamous cell carcinomas in areas of the body that were not exposed to the sun. Whether all PUVA-treated patients will be at increased risk for cutaneous carcinogenesis after a longer period of latency has elapsed remains to be determined.

Because of a probable long latent period for carcinogenic effect, younger persons are at greater risk for long-term side effects. For this reason, the Committee on Drugs of the American Academy of Pediatrics has recommended that children not be enrolled in PUVA treatment programs.

A further concern relating to ocular damage following PUVA exposure is based on animal experiments. The exact length of time that photoactive psoralen remains in the lens of the eye is not known. Because of a risk of cataract formation, eyes must be carefully protected with UVA-blocking sunglasses from time of ingestion of psoralen throughout the active treatment program according to published guidelines. During treatment in the light unit, UVA-opaque goggles are worn.

PUVA therapy of psoriasis remains investigational. In selected patients with severe disabling

psoriasis that has been resistant to conventional therapy, PUVA treatment may be administered according to established guidelines with proper precautions taken to minimize potential toxicity to the skin and eyes.

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ANA-Negative Systemic Lupus Erythematosus

THE PRESENCE OF antinuclear antibodies (ANA) is generally held to be an important criterion in the diagnosis of systemic lupus erythematosus (SLE). However, careful reading of the literature shows a well-described but generally neglected small group of patients with clinical SLE and negative ANA reactions.

In 1978 Fessel reported on ten patients (whose cases had been followed for ten years) with clinical signs of disease but persistently negative reactions to ANA. Each of the ten met at least four of the American Rheumatism Association (ARA) criteria for diagnosis of systemic lupus erythematosus. He noted that Raynaud phenomenon, loss of hair and ulcers of the mouth were more common in ANA-negative patients. It is noteworthy that these signs are all unlikely to be caused by immune complex deposition. However, only one of the ten patients had kidney involvement.

Other studies show similar findings. Pollak in 1964 obtained negative results in 9 patients among 112 with SLE. He summarized the results previously reported in seven other studies containing a total of 274 patients. He noted 7 percent of patients with negative tests for ANA. In the same year, Leonhardt reported that 3 of his 71 patients with SLE had negative tests for ANA. In 1968 Zeiman and co-workers reported clinicopathologic correlation in patients with lupus nephritis; 7 percent of their 28 patients had persistently negative tests for ANA. Estes and Christian obtained negative results in 13 percent of their 150 patients. In 1974 Bartholomew observed that 5 of 121 patients had negative ANA. In 1977 Lee and co-workers noted 5 patients with negative ANA among 110 patients followed for up to five years.

ANA-negative systemic lupus erythematosus seems to be a subgroup of SLE that has not previously been given adequate attention. Raynaud phenomenon, excessive loss of hair and ulcers of the mouth are frequent in this subgroup and the patients are noted to have had prolonged survival. Whether the ANA reaction is negative because of absent production of ANA, because of their in vivo binding by tissues or because of their being hidden in circulating immune complexes, warrants further study. In the meantime, it is important that clinicians be aware that approximately 5 percent of patients with SLE may have persistently negative tests for ANA.

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New Pustular Dermatoses of Infants

TWO NEW FORMS of cutaneous eruptions with unknown causes have been described recently in infants.

Infantile acropustulosis is an uncommon syndrome that consists of recurrent crops of pruritic papulopustules and papulovesicles 1 to 2 mm in size occurring on the distal extremities. Although this dermatosis may be present in infants at birth, it generally begins between the ages of 2 and 10 months, and may persist for two to three years before spontaneous remission occurs. This condition predominates in black infants, and there is no family history of atopy or psoriasis.

The primary lesion is a pinpoint erythematous papule which enlarges to a well-circumscribed and discrete pustule or vesicle within 24 hours. There is no tendency to coalesce. New crops of intensely pruritic vesicopustules appear for a week to ten days, then remit for an interval of two to three weeks before recurring. Most of the lesions are distributed on the palms and soles, with lesser numbers on the dorsa of the hands, wrists, feet and ankles. The eruption is said to be worse in the summer.

Histological examination of infantile acropustulosis shows nonspecific subcorneal or intraepidermal vesicles and pustules which are filled with neutrophilic polymorphonuclear leukocytes and rare eosinophils. Results of routine laboratory